SEQUENCE LISTING

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PRICKETT, KATHRYN S.

<120> INOTROPIC AND DIURETIC EFFECTS OF GLP-1 AND GLP-1 AGONISTS

<130> 256-152DIV US

<140>
<141>

<160> 75

<170> PatentIn Ver. 2.1

<210> 1
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<212> PRT
<213> Heloderma horridum

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His Ser Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu
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Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

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<223> Exendin-4

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His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro Ser
35

<210> 3
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<213> Homo sapiens

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<223> GLP-1

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His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
20 25 30

<210> 4
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<223> Ala or Val

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<223> Ala or Leu

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<223> Pro, homoproline, 3Hyp, 4Hyp, thioproline, N-alkylglycine N-alkylpentylglycine or N-alkylalanine

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<223> Pro, homoproline, 3Hyp, 4Hyp, thioproline, N-alkylglycine N-alkylpentylglycine or N-alkylalanine

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<223> provided no more than three of Xaa3, Xaa5, Xaa6, Xaa8, Xaa10, Xaa11, Xaa12, Xaa13, Xaa14, Xaa15, Xaa16, Xaa17, Xaa19, Xaa20, Xaa21, Xaa24, Xaa25, Xaa26, Xaa27 or Xaa28 are Ala; and the compound is not exendin-3 or exendin-4

<220>
<223> this peptide may encompass 28-39 residues, wherein residues 1-28 are constant and residues 29-39 may vary in length according to the specification

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Xaa Xaa Xaa Gly Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
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Xaa Ala Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa Xaa
20 25 30

Xaa Xaa Xaa Xaa Xaa Xaa Xaa
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His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu
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Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly
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<210> 6
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Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn
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1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
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GLP-1 agonist

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His Ala Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
20 25

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1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
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His Gly Glu Gly Thr Ala Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu
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Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
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His Gly Glu Gly Thr Phe Thr Ala Asp Leu Ser Lys Gln Leu Glu Glu
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Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
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Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
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1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
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Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
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Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
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Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
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His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Ala Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
20 25

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Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
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Ala Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
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1 5 10 15

Glu Ala Ala Arg Leu Phe Ile Glu Phe Leu Lys Asn
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1 5 10 15

Glu Ala Val Ala Leu Phe Ile Glu Phe Leu Lys Asn
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Glu Ala Val Arg Ala Phe Ile Glu Phe Leu Lys Asn
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Glu Ala Val Arg Leu Phe Ile Glu Ala Leu Lys Asn
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Glu Ala Val Arg Leu Phe Ile Glu Phe Ala Lys Asn
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Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Ala Asn
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1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Ala
20 25

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His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu
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Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
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Ser Gly Ala Pro Pro Pro
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Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro Pro
35

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Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
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Ser Gly Ala Pro Pro
35

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Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro Pro
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Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser Gly Ala Pro
35

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Ser Gly Ala Pro
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Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
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Ser Gly Ala
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Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser Gly Ala
35

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GLP-1 agonist

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Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser Gly

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Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser Gly

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GLP-1 agonist

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<400> 38
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1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser

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GLP-1 agonist

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<400> 39
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1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser

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1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

<210> 41
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Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser
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1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro
20 25 30

<210> 43
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1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro
20 25 30

<210> 44
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<400> 44
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1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly
20 25 30

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1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly
20 25

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GLP-1 agonist

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1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly
20 25

<210> 47
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His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Xaa Ser
20 25 30

Ser Gly Ala Xaa Xaa Xaa

35

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Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser Gly Ala Xaa Xaa Xaa
35

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His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu
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Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Xaa Ser
20 25 30

Ser Gly Ala Pro Pro
35

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Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Xaa Ser
20 25 30

Ser Gly Ala Xaa Xaa
35

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His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Xaa Ser
20 25 30

Ser Gly Ala Xaa Xaa
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<220>
<221> MOD_RES
<222> (36)
<223> hPro

<220>
<223> C-term amidated

<400> 52
His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Xaa Ser
20 25 30

Ser Gly Ala Xaa
35

<210> 53
<211> 35
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Exendin or
GLP-1 agonist

<220>
<223> C-term amidated

<400> 53
Arg Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser Gly Ala
35

<210> 54
<211> 30
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Exendin or
GLP-1 agonist

<220>
<223> C-term amidated

<400> 54
His Gly Asp Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly
20 25 30

<210> 55
<211> 28
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Exendin or GLP-1 agonist

<220>
<221> MOD_RES
<222> (6)
<223> Naphthylala

<220>
<223> C-term amidated

<400> 55
His Gly Glu Gly Thr Xaa Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
20 25

<210> 56
<211> 28
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Exendin or GLP-1 agonist

<220>
<223> C-term amidated

<400> 56
His Gly Glu Gly Thr Phe Ser Ser Asp Leu Ser Lys Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn
20 25

<210> 57
<211> 28
<212> PRT
<213> Artificial Sequence

<220>

<223> Description of Artificial Sequence: Exendin or
GLP-1 agonist

<220>
<223> C-term amidated

<400> 57
His Gly Glu Gly Thr Phe Ser Thr Asp Leu Ser Lys Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn
20 25

<210> 58
<211> 28
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Exendin or
GLP-1 agonist

<220>
<223> C-term amidated

<400> 58
His Gly Glu Gly Thr Phe Thr Ser Glu Leu Ser Lys Gln Met Ala Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn
20 25

<210> 59
<211> 28
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Exendin or
GLP-1 agonist

<220>
<221> MOD_RES
<222> (10)
<223> pentylgly

<220>
<223> C-term amidated

<400> 59
His Gly Glu Gly Thr Phe Thr Ser Asp Xaa Ser Lys Gln Leu Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn
20 25

<210> 60
<211> 28
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Exendin or
GLP-1 agonist

<220>
<221> MOD_RES
<222> (22)
<223> Naphthylala

<220>
<223> C-term amidated

<400> 60
His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Xaa Ile Glu Phe Leu Lys Asn
20 25

<210> 61
<211> 28
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Exendin or
GLP-1 agonist

<220>
<221> MOD_RES
<222> (23)
<223> tButylgly

<220>
<223> C-term amidated

<400> 61
His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Xaa Glu Trp Leu Lys Asn
20 25

<210> 62
<211> 28
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Exendin or
GLP-1 agonist

<220>
<223> C-term amidated

<400> 62
His Gly Glu Gly Thr Phe Thr Ser Asp Leu Ser Lys Gln Leu Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Asp Phe Leu Lys Asn

20 25

<210> 63
<211> 33
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Exendin or GLP-1 agonist

<220>
<223> C-term amidated

<400> 63
His Gly Glu Gly Thr Phe Thr Ser Asp Ala Ser Lys Gln Leu Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Phe Leu Lys Asn Gly Gly Pro Ser
20 25 30

Ser

<210> 64
<211> 29
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Exendin or GLP-1 agonist

<220>
<223> C-term amidated

<400> 64
His Gly Glu Gly Thr Phe Thr Ser Asp Ala Ser Lys Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly
20 25

<210> 65
<211> 37
<212> PRT
<213> Artificial Sequence

<220>
<223> Description of Artificial Sequence: Exendin or GLP-1 agonist

<220>
<221> MOD_RES
<222> (31)
<223> hPro

<220>
<221> MOD_RES
<222> (36)..(37)

<223> hPro

<220>
<223> C-term amidated

<400> 65
His Gly Glu Gly Thr Phe Thr Ser Asp Ala Ser Lys Gln Met Glu Glu
1 5 10 15

Glu Ala Val Arg Leu Phe Ile Glu Trp Leu Lys Asn Gly Gly Xaa Ser
20 25 30

Ser Gly Ala Xaa Xaa
35

<210> 66
<211> 29
<212> PRT
<213> artificial sequence

<220>
<223> Agonist of GLP-1

<220>
<221> MOD_RES
<222> (1)..(1)
<223> Ala is modified with an R group which can be 4-imidazopropionyl (des-amino-histidyl), 4-imidazoacetyl, or 4-imidazo-a, adimethyl-acetyl

<220>
<221> MOD_RES
<222> (19)..(19)
<223> Xaa is a Lys or Arg

<220>
<221> misc_feature
<222> (19)..(19)
<223> Xaa can be any naturally occurring amino acid

<220>
<221> MOD_RES
<222> (27)..(27)
<223> Lys is modified with an R group consisting of C6 -C10 unbranched acyl, or is absent

<220>
<221> MOD_RES
<222> (29)..(29)
<223> Arg is modified with an R group consisting of Gly-OH or NH2

<400> 66

Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly Gln
1 5 10 15

Ala Ala Xaa Glu Phe Ile Ala Trp Leu Val Lys Gly Arg
20 25

<210> 67
<211> 19
<212> PRT
<213> artifical sequence

<220>
<221> MOD_RES
<222> (1)..(1)
<223> Ser is modified by H2N, H2N-Ser, H2N-Val-Ser, H2N-Asp-Val-Ser. or any one of SEQ ID NO:68 to 74

<220>
<221> MOD_RES
<222> (17)..(17)
<223> Xaa is a Lys or Arg

<220>
<221> misc_feature
<222> (17)..(17)
<223> Xaa can be any naturally occurring amino acid

<220>
<221> MOD_RES
<222> (19)..(19)
<223> Arg can be modified by the group consisting of NH2, OH, Gly-NH2, or Gly-OH

<400> 67

Ser Tyr Leu Glu Gly Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val
1 5 10 15

Xaa Gly Arg

<210> 68
<211> 4
<212> PRT
<213> artificial sequence

<220>
<223> variable sequence insert for artificial GLP-1 analog

<400> 68

Ser Asp Val Ser
1

<210> 69
<211> 5
<212> PRT
<213> artificial sequence

<220>
<223> variable sequence insert for artificial GLP-1 analog

<400> 69

Thr Ser Asp Val Ser

1 5

<210> 70
<211> 6
<212> PRT
<213> artificial sequence

<220>
<223> variable sequence insert for artificial GLP-1 analog

<400> 70

Phe Thr Ser Asp Val Ser
1 5

<210> 71
<211> 7
<212> PRT
<213> artificial sequence

<220>
<223> variable sequence insert for artificial GLP-1 analog

<400> 71

Thr Phe Thr Ser Asp Val Ser
1 5

<210> 72
<211> 8
<212> PRT
<213> artificial sequence

<220>
<223> variable sequence insert for artificial GLP-1 analog

<400> 72

Gly Thr Phe Thr Ser Asp Val Ser
1 5

<210> 73
<211> 9
<212> PRT
<213> artificial sequence

<220>
<223> variable sequence insert for artificial GLP-1 analog

<400> 73

Glu Gly Thr Phe Thr Ser Asp Val Ser
1 5

<210> 74
<211> 10
<212> PRT
<213> artificial sequence

<220>
<223> variable sequence insert for artificial GLP-1 analog

<400> 74

Ala Glu Gly Thr Phe Thr Ser Asp Val Ser
1 5 10

<210> 75
<211> 29
<212> PRT
<213> artificial sequence

<220>
<223> artificial

<220>
<221> MOD_RES
<222> (1)..(1)
<223> neurtal amino acid or D or N-acylated or alkylated form of histidine can be substituted for His

<220>
<221> MOD_RES
<222> (2)..(2)
<223> small neutral amino acid can be substituted for Ala

<220>
<221> MOD_RES
<222> (3)..(3)
<223> acidic or neutral amino acid can be substituted for Glu

<220>
<221> MOD_RES
<222> (4)..(4)
<223> neutral amino acid can be substituted for Gly

<220>
<221> MOD_RES
<222> (9)..(9)
<223> acidic amino acid can be substituted for Asp

<220>
<221> MOD_RES
<222> (10)..(10)
<223> Tyr can be substituted for Val

<220>
<221> MOD_RES
<222> (12)..(12)
<223> Lys can be substituted for Ser

<220>
<221> MOD_RES
<222> (15)..(15)
<223> Asp can be substituted for Glu

<220>
<221> MOD_RES
<222> (16)..(16)

<223> Ser can be substituted for Gly

<220>
<221> MOD_RES
<222> (17)..(17)
<223> Arg can be substituted for Gln

<220>
<221> MOD_RES
<222> (18)..(18)
<223> Arg can be substituted for Ala

<220>
<221> MOD_RES
<222> (20)..(20)
<223> Lys can be substituted for a neutral amino acid, arg, or a D form of lys

<220>
<221> MOD_RES
<222> (20)..(20)
<223> Gln can be substituted for Lys

<220>
<221> MOD_RES
<222> (25)..(25)
<223> Trp can be substituted for an oxidation-resistant amino acid

<220>
<221> MOD_RES
<222> (28)..(28)
<223> Lys can be substituted for a neutral amino acid, arg, or a D form of lys

<220>
<221> MOD_RES
<222> (29)..(29)
<223> Xaa is a Gly, Gly-Arg, Gly-Arg-Gly, or absent

<220>
<221> misc_feature
<222> (29)..(29)
<223> Xaa can be any naturally occurring amino acid

<400> 75

His Ala Glu Gly Thr Phe Thr Ser Asp Val Ser Ser Tyr Leu Glu Gly
1 5 10 15

Gln Ala Ala Lys Glu Phe Ile Ala Trp Leu Val Lys Xaa
20 25